- **Histology of a lymph node:**
  - They are bean-shaped structures with a concave side know as the hilum (into which arteries, veins, nerves and efferent lymphatic vessels enter).
 - They aid in the filtration of lymph.
  - A lymph node is covered with a capsule which is penetrated by afferent lymphatic vessels.
  - **The interior is divided into:**
    - ✓ *Cortex*: which is made up of lymphatic nodules (with outer dark staining area and inner light staining area) containing B-lymphocytes.
    - ✓ *Para-cortex (deep cortex)*: which is composed of T-lymphocytes.
    - ✓ *Medulla*: which is composed of medullary cords (containing lymphocytes, macrophages and plasma cells) and medullary sinuses (which empty their lymph into the efferent lymphatics).

      Note: most lymphocytes enter the lymph node through specialized High Endothelial Venules (HEVs). Only 10% of lymphocytes will enter the lymph node through afferent lymphatic vessels.
  - **If there is an early metastasis of cancer** in the body from an organ to a lymph node → it will appear first in the sub-capsular sinus of the lymph node.
  - **A tingible-body macrophage** is a type of macrophage predominantly found in germinal centers of the lymph nodes. It contains many phagocytized apoptotic cells in various states of degradation referred to as tangible bodies. If these macrophages are not seen, follicular lymphoma is suspected.
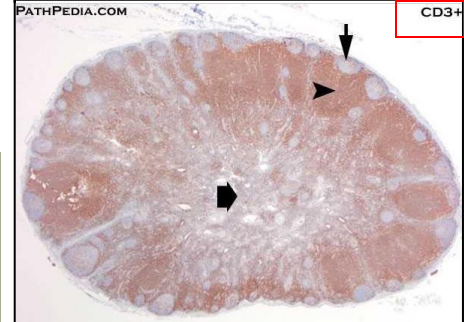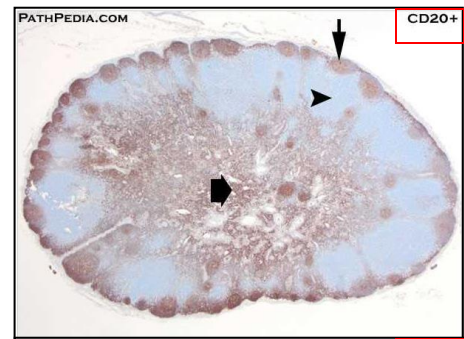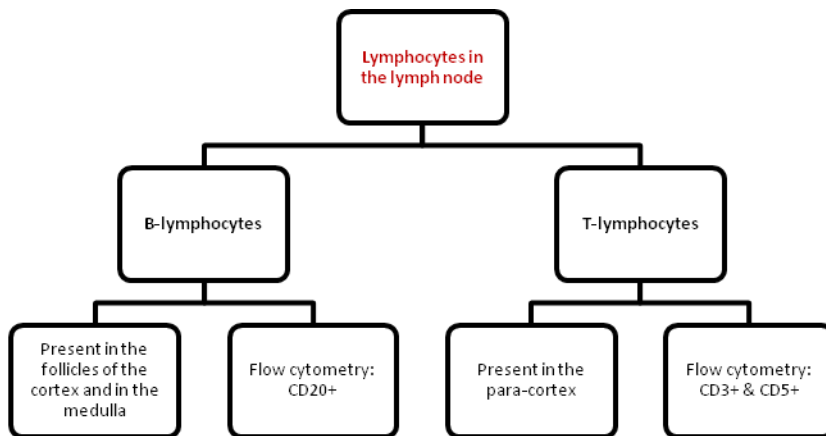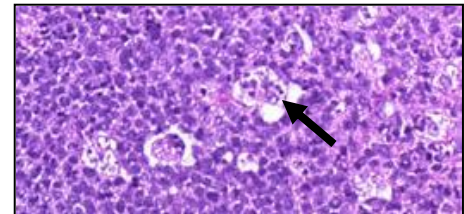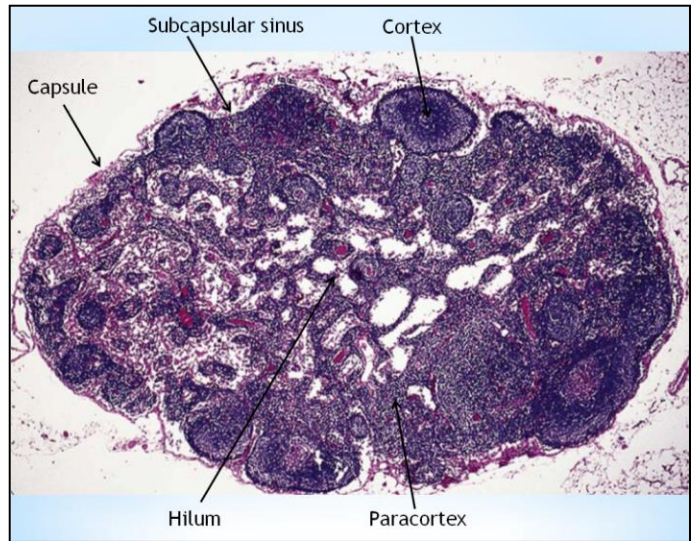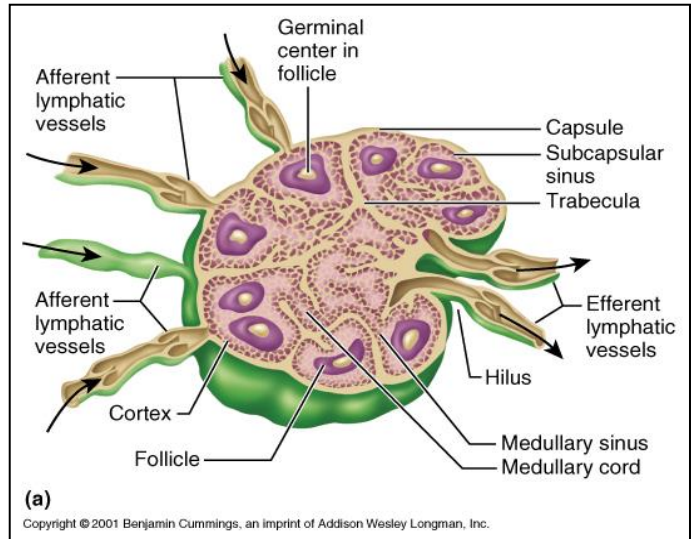

Staining is done to detect the presence of specific CD markers (to know the type of lymphocytes in the lymph node). Blue stain means a negative result for the presence of the CD marker. Brown stain means a positive result for the presence of the CD marker.

- **Lymphoid neoplasms include:**
  - Lymphocytic leukemias.
  - Lymphomas.
  - Plasma cell neoplasms.

  Note: the clinical feature of lymphomas overlap and classification is based on morphologic and molecular characteristics of the tumor cells.
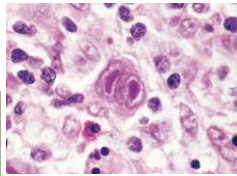

Classification of lymphomas

Lymphoma: a tumor arising from lymphocytes no matter if they are in the lymph nodes or outside them

- Hodgkin lymphoma
- Non-hodgkin lymphoma

- Classical
- Lymphocyte predominant

- Nodular sclerosis
- Mixed-cellularity
- Lymphocyte-rich
- Lymphocyte depleted

- **Reed-sternberg cells (figure):**
  - They are different giant cells found with light microscopy in biopsies from individuals with classical Hodgkin lymphoma. They are usually derived from B-lymphocytes, classically considered crippled germinal center B-cells, meaning they have not undergone hypermutation to express their antibodies.
  - RS-cells: large, multilobate nucleus (two mirror image nuclear lobes, each containing a large acidophilic nucleolus surrounded by a clear zone) and they are present in a background of mixed reactive inflammatory cells.
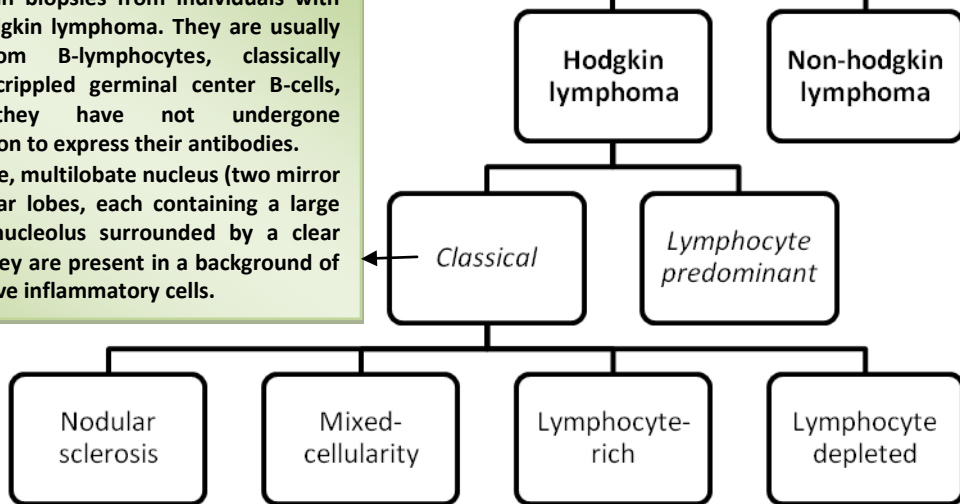
- **To classify lymphomas** → immune-histo-chemistry (IHC) and flow cytometry must be done (both together, one of them is not enough!).
- B-cells: their early stages of development will be in the bone marrow. Then, they will be secreted in the periphery where they will travel to lymph nodes to be exposed to antigens. During maturation of B-lymphocytes, different markers will appear and disappear from the surface of the cells. When there is lymphoma, flow cytometry will be done and the detected marker on the cell surface will reflect in which cell stage is this type of lymphoma (ex. If TDT is found → lymphoblastic lymphoma). The same principle applies on T-cells.
- **Classical Hodgkin lymphoma:**
  - **NODULAR SCLEROSIS:**
    - ✓ *Histologic features*: there are multiple nodules (figure) surrounded by collagen bands of fibrosis resulting in sclerosis. The RS-cells will be present and called lacunar cells (figure).
    - ✓ *Frequency*: 60-80% - more common in women.
    - ✓ *Prognosis*: good – most are stage I or II.
  - **MIXED-CELLULARITY:**
    - ✓ *Histologic features*: a sheet composed of many different cells.
    - ✓ *Frequency*: 15-30% - more common in older adults.
    - ✓ *Prognosis*: fair – most are stage III.
  - **LYMPHOCYTE-RICH:**
    - ✓ *Histologic features*: mostly reactive lymphocytes and many RS-cells.
    - ✓ *Frequency*: 5% - older adults.
    - ✓ *Prognosis*: good-excellent.
  - **LYMPHOCYTE-DEPLETED:**
    - ✓ *Histologic feature*: many RS-cells and variants.
    - ✓ *Frequency*: less than 1% - rare.
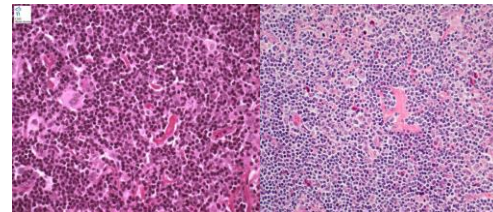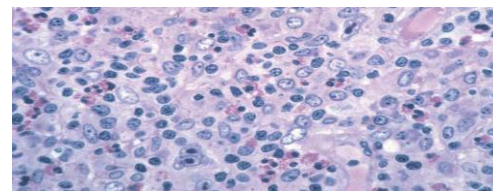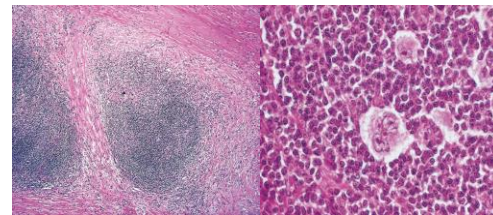
✓ *Prognosis*: poor – most are stage III or IV.
- <u>**Classical Hodgkin lymphoma features/characteristics:**</u>
  - The RS-cells and variants are CD15+ and CD30+
  - EBV is present in the RS-cells in 70% of cases of mixed-cellularity subtype and smaller fraction of other classical subtypes.
  - The background is generated by cytokines secreted by RS-cells:
    - ✓ IL-5: attracting eosinophils.
    - ✓ TGF-β: fibrogenic factor.
- <u>**Lymphocyte predominance Hodgkin lymphoma:**</u>
  - **Characterized by**: the presence of lyphohistiocytic cells (L&H cells). These cells have a delicate multilobated nucleus resembling popped corn (popcorn cell). The background in which L&H cells are found is made up of B-cells.
  - L&H cells are CD45+, CD20+ (B-cells marker).
  - Not related to EBV.
  - Patients present with isolated cervical or axillary lymphadenopathy.
  - **Prognosis**: excellent.